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REVIEW ARTICLE

An overview on phytoconstituents and multiple biological activities of *Euphorbia hirta* Linn.

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Abstract

The major genus in the Euphorbiaceae family, Euphorbia is having more than 1600 species. The Euphorbiaceae family includes the annual weed *Euphorbia hirta*, sometimes referred to as the asthma plant. It's not just a weed, it also has medical properties. The Chinese Pharmacopoeia and African pharmacopoeia listed *E. hirta* for many drugs. Along with tropical and temperate regions of the world, Africa, Bangladesh, Australia and India are also home to these therapeutic herbs. The current review discusses its phytoconstituent profile, therapeutic profile and other significant biological characteristics. It includes a number of secondary active compounds, such as polyphenols, flavonoids, steroids, tannins and alkaloids, which act as anti -microbial, anti-fertility, anti-diabetic, anti-inflammatory, anti-cancer, anti-plasmodial, anti-tumor and in the management of many other disorders. Hematuria and gonorrhoea are also treated with *E. hirta*. In South Africa *E. hirta* is widely accepted as the prophylaxis of asthma. The herb is utilized as an enema remedy in the Gold Coast. Inflammatory bowel disease, psoriasis and diabetic-induced sores are just a few of the chronic inflammatory disorders that can be treated topically using the alcohol-based fruit and leaf extract of *E. hirta*. For the purpose of identifying and creating a monograph on *E. hirta*, this review may be used.

Keywords

Euphorbia hirta Linn., phytochemistry, traditional uses, ethnopharmacological roles, pharmacologically

Introduction

Since ancient times, it has been popular in India to employ various medicinal plant components to treat particular illnesses. The indigenous medical systems, including Ayurvedic, Siddha and Unani, have been practiced for many years. Ayurvedic medicines that target contemporary ailments are already available on the market (1). The most popular and widely recognized kinds of medications today are herbal ones. The principal source of herbal medicinal products comes from a variety of secondary active metabolites that the plant creates and biosynthesizes from primary metabolites. Euphorbiaceae is among the most widely accepted family which is utilized to treat various human disorders. The major genus in the Euphorbiaceae family, *Euphorbia* is having more than 1600 species. The presence of more or less poisonous white milky latex serves as a defining characteristic. Plants of this group have been the focus of extensive phytochemical research including the isolation of chemicals such as flavonoids, alkanes,

triterpenoids, alkaloids, tannins and amino acids (2). The entire plant is typically used to treat a variety of illnesses, primarily gastrointestinal disorders, complaints of the skin and mucous membranes and breathing apparatus issues. It is a widely utilized component of traditional Chinese medicine and local traditional medicine in clinical research (3).

Materials and Methods

Using terms like Euphorbiaceae, *E. hirta*, management, conservative treatment and surgical procedure, a large database of several diverse web sites was browsed through. This study discusses the botanical description, traditional uses, ethnopharmacological role, phytochemistry, various pharmacological roles and toxicology of *E. hirta*. Several articles from several websites, including Google Scholar, Springer, Taylor and Francis, Elsevier and Bentham are studied for the literature survey.

General information about Euphorbia hirta

Taxonomical Classification

Kingdom	:	Plantae
Subkingdom	:	Viridaeplantae
Infrakingdom	:	Straptophyta
Division	:	Tracheophyta
Subdivision	:	Spermatophytina
Infradivision	:	Angiosperms
Class	:	Magnoliopsida
Superorder	:	Rosanae
Order	:	Malpighiales
Family	:	Euphorbiaceae
Genus	:	*Euphorbia*
Species	:	*Euphorbia hirta (Euphorbia pilulifera)*

China, Arab, Malaysia, Indonesia, Malay, Sundan, New Britain, Philippines, Laos, Thailand, Vietnam, France, India, Bangladesh, Japan, Norway, Australia and Liberia are just a few of the nations where *E. hirta* has been distributed. Other common names for *E. hirta* are included in Table 1 in many other languages.

Botanical Description

Plant Part Details

Annual herb ±60 cm, stem reddish or purple, hairy and produces latex (Fig. 1).

Leaves

Opposite, distichous, elliptical or ovate-lanceolate, long elliptic, lanceolate-oblong or serrated. The apex is sharp and one side is wedge-shaped while another one is obliquely rounded (Fig. 1) (4).

Table 1. Common names of *Euphorbia hirta* in various languages

Language	Common names
English	Asthma weed, Cats hair, Pill-Bearing Spurge , Snakeweed, Dove milk, Asthma weed, Common spurge, Cats hair
Hindi	Bara dudhi
Manipuri	Pakhangleiton, Pakhangbamaton
Marathi	Dudhi
Tamil	Ammam Paccharisi
Malayalam	Nelapala
Telugu	Nanabalu
Bengali	Barokarni
Konkani	Dudurli
Tangkhul	Pakhangleiton
Nepali	AnkhleJhaar,Dudhe, DudheJhaar, Dudhiyaa
Assamese	Gakheerotee bon
Mizo	Zawhte-hlo

Fig. 1. *E. hirta* plant parts.

Flowers

Monoecious, terminal or axillary "cyathium," which is made up of several cyathia. Both female and male flowers are found which are apetalous. The blooms are unisexual; the female flowers feature a small pedicel, a ringed perianth, a superior ovary with 3 little styles and a 2-fold apex and a 3-celled structure. The perianth is missing, the bracteoles are linear and fringed and there is just one stamen on the male flowers. Typically, flowers are in bloom all year long (5).

Stem

The stems with monopodial branching pattern. Stipules present, internodes extending upto 2.5 to 3 cm (Fig. 1) (6).

Fruit

Pistillate, allomorphic, elongated, trilobated, an abbreviate base with tiny hairs. Capsule 3-seeded, green and coated in

fleshy prickles (8). Seeds rectangular, 4-sided kaleidoscopic, shrivelled, chestnut pink, with a white caruncle at the tip that encloses an oily endosperm (9).

Root

It has a unique and evolved tap root system for its main root (7).

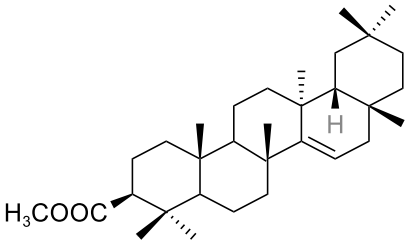
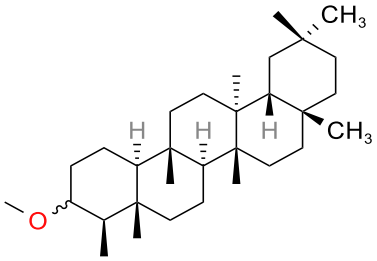
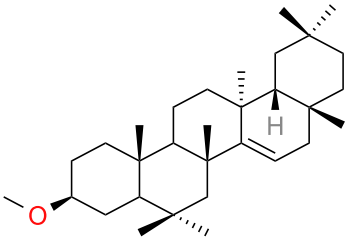
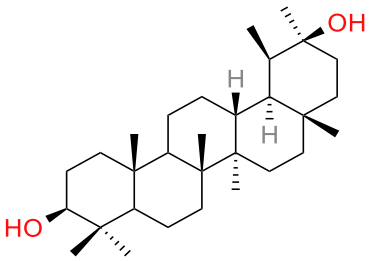
Ethnopharmacological Applications

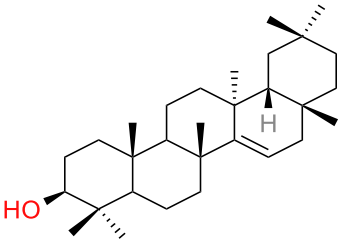
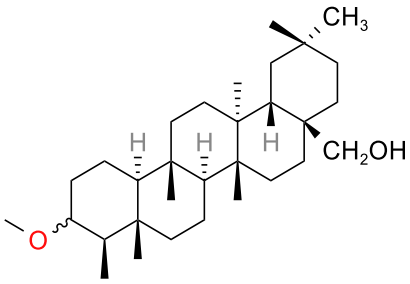
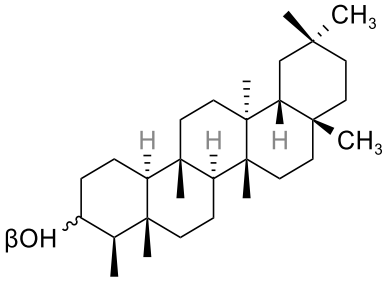
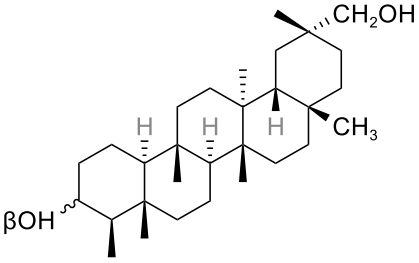
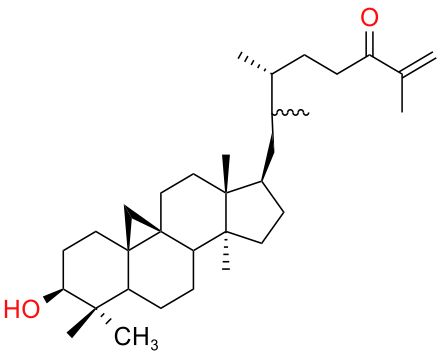
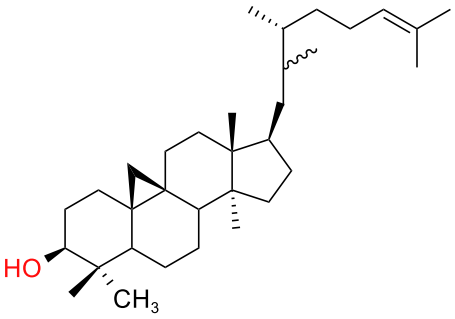
The use of *E. hirta* as a medicine is widespread across the world (3). There are several different pharmacological formulations employed, including juice, decoction, infusion and dry powders (4). It was used to treat various gastrointestinal disorders (bowel complaints, constipation, dysentery and digestive problems), thoracic and other respiratory diseases (emphysema, allergic rhinitis, asthma, bronchitis, whoop and cold) and inflammation of conjunctiva, to increase lactation in nursing women and for other female diseases. Due to its extensive variety of biological and pharmacological actions, it is utilised in ethnomedicine (7). The Chinese Pharmacopoeia and African pharmacopoeia listed *E. hirta* for many drugs (8). Animals with stomach flu and diarrhoea are also treated with the crude extracts of the complete plant in conventional medicine (9). Used also for hematuria and gonorrhoea. The plant's roots were used to treat wrench and inflammation, epilepsy, stillbirth, worms in wounds and hyperdontia. In India, it is used to treat tumours, diarrhoea, gonorrhoea, jaundice, acne and childhood worm infections. On wounds and warts, the fresh milky latex was applied. Flowers, stems and leaves are employed as medicinal components (9). In South Africa, *E. hirta* is widely accepted as prophylaxis of asthma. The herb is utilized as an enema remedy in the Gold Coast (10). The leaves are used in Indian traditional medical systems to cure kidney stones, syphilis, asthma, bronchial infections, digestive issues, wound healing and cough, cold and fever. The latex is used to treat ulcers and conjunctivitis (11).

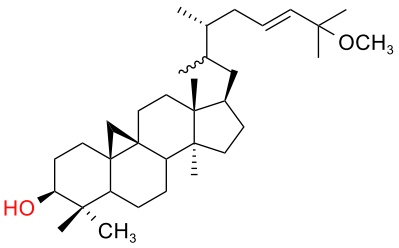
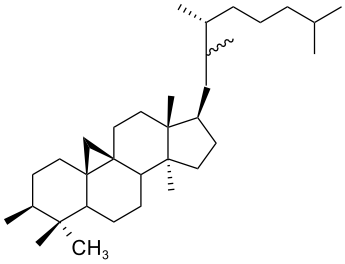
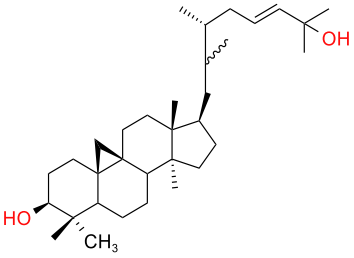
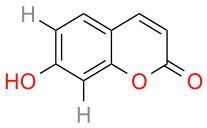
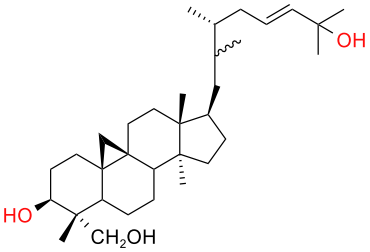
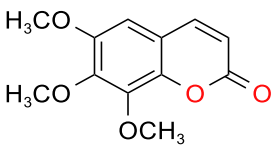
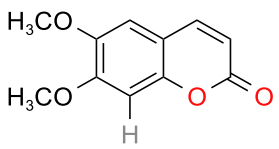
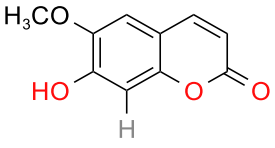
Phytochemistry

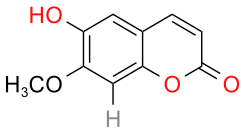
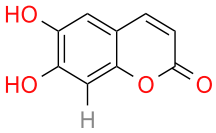
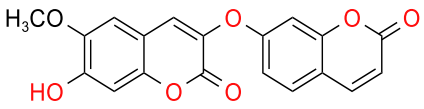
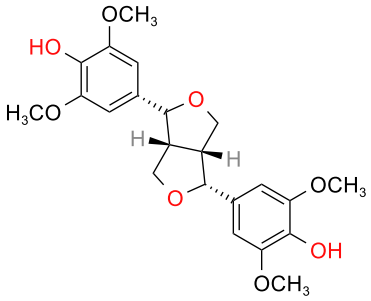
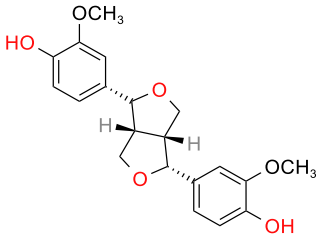
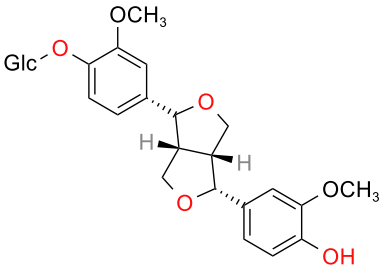
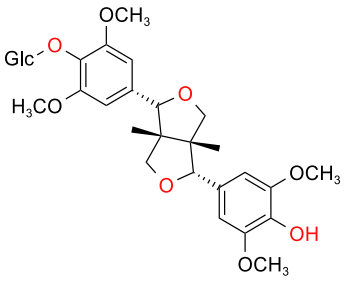
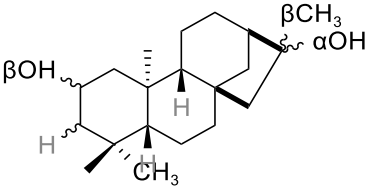
E. hirta contains triterpenoids (oleanane type, ursane skeleton, friedelane compounds, cycloartane ones), coumarins, lignans and diterpenes. Table 2 listed many phytoconstituents that were found in the plant *E. hirta* (1, 12).

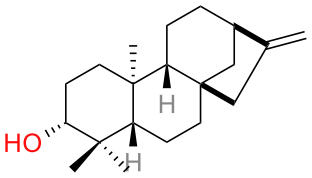
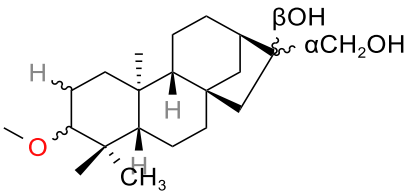
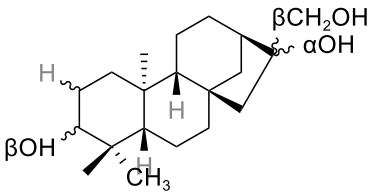
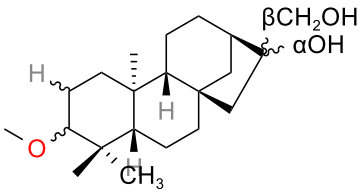
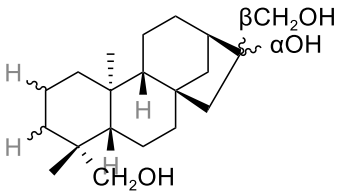
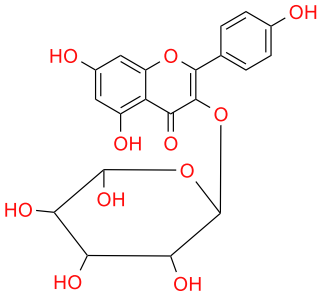
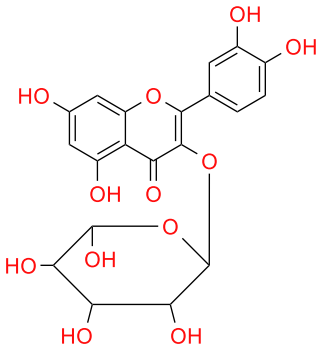
Table 2. Various Chemical Constituents present in *Euphorbia hirta*

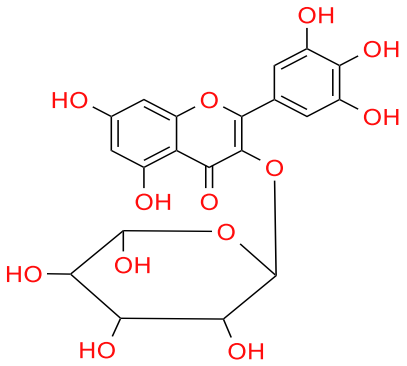
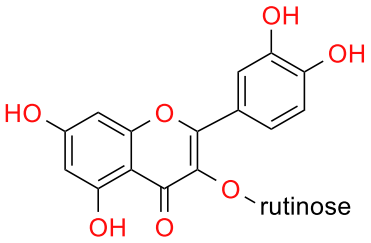
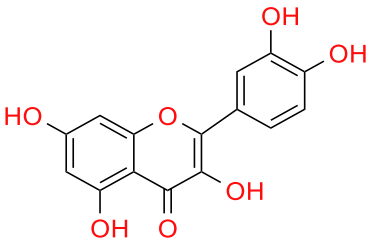
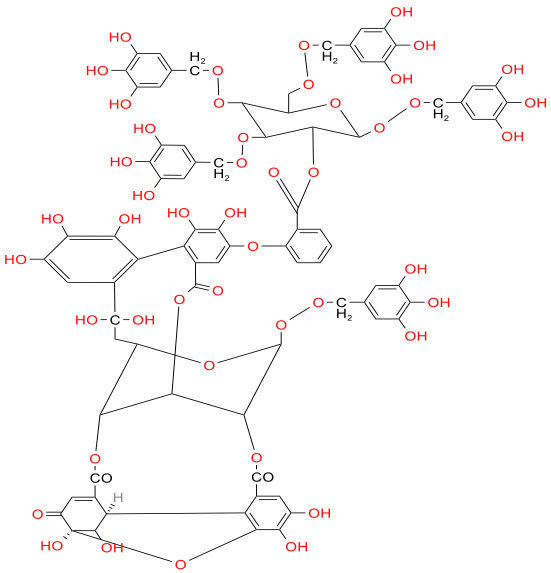
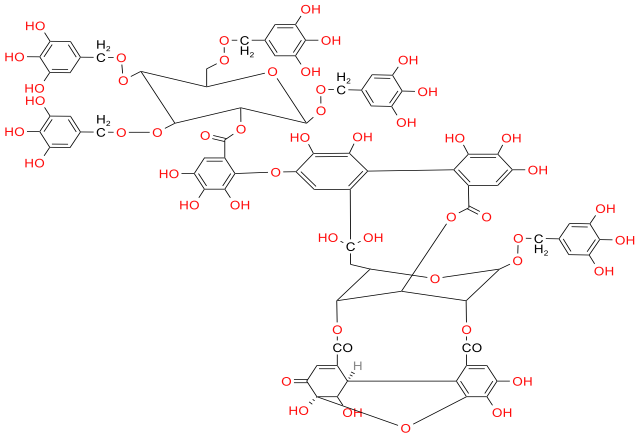
S. No.	Chemical Name	Chemical constituent type	Structure
1	Taraxerol acetate	Triterpenoids	
2	Friedelin	Triterpene	
3	Taraxerone	Scalarane sesterterpenoid	
4	ϕ-taraxastane-3,20-diol	Triterpenoids	

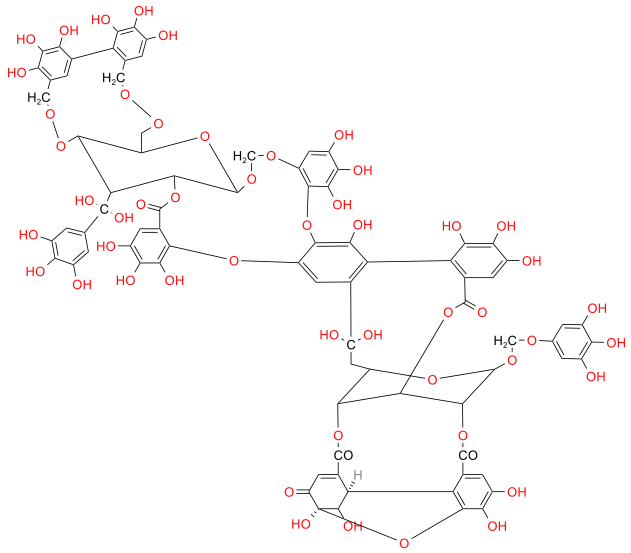
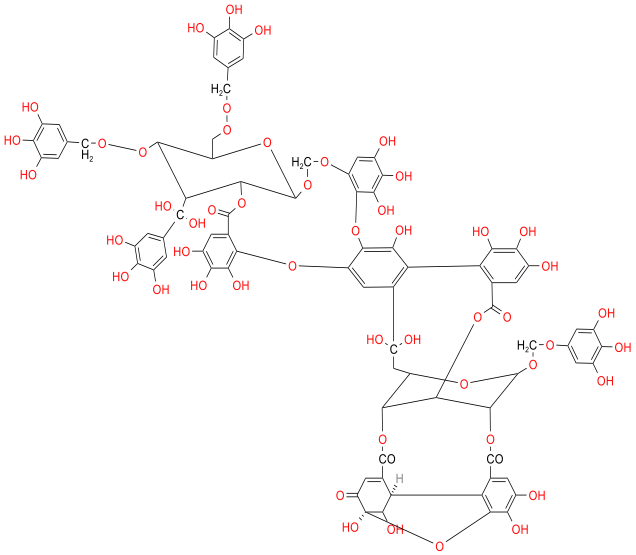
5	Taraxerol	Pentacyclic Triterpenoids	
6	28-hydroxyfriedelin	Triterpene	
7	Friedelan-3β-ol	Triterpene	
8	Friedelane-3β,29-diol	Triterpene	
9	3β-hydroxy-cycloart-25 -ene-24-one	Triterpenoids	
10	Cycloartenol	Pentacyclic Triterpenoids	

11	23(*E*)-25-methoxycycloart-23-en-3β-ol	Triterpenoids	
12	Cyclolanostan-3β-ol	Triterpenoids	
13	Cycloart-23-ene-3β,25-diol	Triterpenoids	
14	Umbelliferone	7-hydroxycoumarin	
15	Cycloart-23-ene-3β,25,28-triol	Triterpenoids	
16	6,7,8-trimethoxyl-coumarin	Natural coumarin	
17	Scoparone	Coumarin derivatives	
18	Isoscopoletin	Coumarin derivatives	

19	Scopoletin	Hydroxycoumarin	
20	Esculetin	Hydroxycoumarin	
21	Daphnoretin	Coumarin derivatives	
22	(+)-syringaresinol	Lignan	
23	(-)-pinoresinol	Tetrahydrofuran Lignan	
24	(-)-pinoresinol glucoside	Lignan and glycoside	
25	(+)-syringaresinol glucoside	Glycoside	
26	2β, 16α, 19-trihydroxy -*ent*-kaurane	Diterpenoids	

27	*ent*-kaur-16-ene-3β-ol	Diterpenoids	
28	16β, 17-dihydroxy-*ent*-kaurane-3-one	Diterpenoids	
29	3β, 16α, 17-trihydroxy-*ent*-kaurane	Diterpenoids	
30	16α, 17-dihydroxy-*ent*-kaurane-3-one	Diterpenoids	
31	16α, 17, 19-trihydroxy-*ent*-kaurane	Diterpenoids	
32	Afzelin	Glycosyloxyflavone	
33	Quercitrin	Quercetin o-glycoside	

34	Myricitrin	Pentahydroxyflavone	
35	Rutin	Rutinoside	
36	Quercitin	Pentahydroxyflavone	
37	Euphorbin-A	Dimeric dehydroellagitannins	
38	Euphorbin-B	Dimeric dehydroellagitannins	

39	Euphorbin-C	Dimeric dehydroellagitannins	
40	Euphorbin-D	Dimeric dehydroellagitannins	

Proximate Characteristics

The proximate properties of *E. hirta* include total ash content of 8.90, acid insoluble ash of 7.84, water-soluble ash of 1.06, water-soluble extract of 7.0, ethanol extract of 14.85, methanol extract of 9.71 and moisture content of 9.84 (percentage w/w). Table 3 listed the physicochemical characteristics of *E. hirta* (2).

Table 3. Physicochemical Properties of the *Euphorbia hirta*

Content	Plant Parts	Percentage w/w
Lipid	Leaves	25
	Stems	14
Carbohydrates	Leaves	1.5
	Stems	8.0
Protein	Leaves	9.5
	Stems	3.0
Ash	Leaves	18.6
	Stems	21.5
Acid insoluble-ash	Leaves	3.5
	Stems	2.5
Moisture content	Leaves	13.5
	Stems	10.3

Pharmacological Roles of Euphorbia hirta

Table 4 lists the many pharmacological functions of the plant parts, together with their extraction form, dosages and induction methods and Fig. 2 shows a graphical representation of pharmacological roles.

Aflatoxin inhibition Property

According to one study, an aqueous extraction of whole plant significantly prevented aflatoxin generation on rice, maize, wheat and peanuts (27).

Anti-hepatoxic activity

Boerhaavia diffusa and *Euphorbia hirta* extracts were tested in experimental models of rat hepatotoxicity brought on by CCL4 or paracetamol. Testing was done on hydroalcoholic extract (HE) from the entire plant. The assessment of many biochemical markers in serum and tissues allowed for the identification of hepatic dysfunction. The aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), alkaline phosphate (ALP) and bilirubin activity in serum were assessed. Lipid peroxidation and decreased glutathione levels in control and treated rats were also examined. Since serum levels of ALT and AST in rats given the extracts were considerably low (p 0.05

Table 4. List of Pharmacological Activities of *Euphorbia hirta L.* Family: Euphorbiaceae.

Sr. No.	Plant part used	Solvents for Extraction	Pharmacological Use	Dose	Experimental Animal	Chemicals	Reference
1.	Leaves	Methanol	Anti-inflammatory	Administrated orally at a dose of 200, 400 and 800 mg/kg in mice	Mice	Diclofenac sodium 100 mg/kg b.wt., xylene 20 μL, chloroform, cotton pellets,	(13)
2.	Whole plant	Lyophilized aq.	Sedative and calming	1) high dose (100 mg/kg & more) 2) lower dose (12. 5 mg & 25 mg of dried plant /kg	Mice	NaCl 0.9% solution, clorazepate dipotassium 1, 5, 10, 20 and 40 mg/kg.	(14)
3.	Whole plant	Lyophilized aq.	Antidiarrhoeal	50 mg/kg against castor oil	Mice, Rat	Flavonoids, glycoside's part aglycone PGE2	(15, 16)
4.	Leaf	Water, ethanol	Diuretic	50 &100 mg/kg	Rat	Furosamide	(17)
5.	Whole plant	Ethanol, Dichloromethane	Antimalarial	100-400 mg/kg/day	Mice	Chloroquine 5 mg/kg	(18)
6.	Whole plant	Polyphonol	Antispasmodic and antiamebic	Cocn. of 80 µg/ml & less conc. 10 pg/ml	Guinea pig ileum	KCl	(19)
7.	Whole plant	Ethanol	Antiplasmodial	Cocn. of 0.5 to 500 µg/ml	*Plasmodium falciparum*	Terpene, flavonoids, steorial, phenolic acid, xanthans, anthraquinones	(20)
8.	Steam, Bark and Leaf	Aq. leaf	Molluscicidal	1) stem bark-sub lethal dose (40% & 80 % of lc50) 2) leaf –p<0. 05	Vector snail *Lymnaea acuminta*	Protein, nuclic acid, free amino acid, alkaline phosphate	(21)
9.	Aerial part	Ethanol	Antimicrobial	Orally at 25, 50, 100 and 200 mg/kg	Bacteria (*E. coil*, *S. aureus*)	Flavonoids	(22)
10.	Leaf	Ethanol	Anticancer, antihistamine, and antipyretic	25 -50, 100 mg/kg 2 hrs before inta-articular inj. of Lipopolysaccharide	Rat	TNF- α	(23)
11.		Ethanol	Inhibits anaphylactic	100-1000 mg/kg	Rat & paw anaphylaxis in mice	TNF- α & IL-6	(24)
12.	Leaf	Leaves	Antidiabetic	300 mg/kg body wt. / rat /day	Rat	Lipid peroxides, hydroperoxide	(25)
13.	Leaf	Methanol	Antioxidant	1 mg/mL	Diphenyl-1-picrylhydrazyl (DPPH) assay	Diphenyl-1-picrylhydraczyl, terpenoids, alkaloids, tannins, flavonoids.	(26)

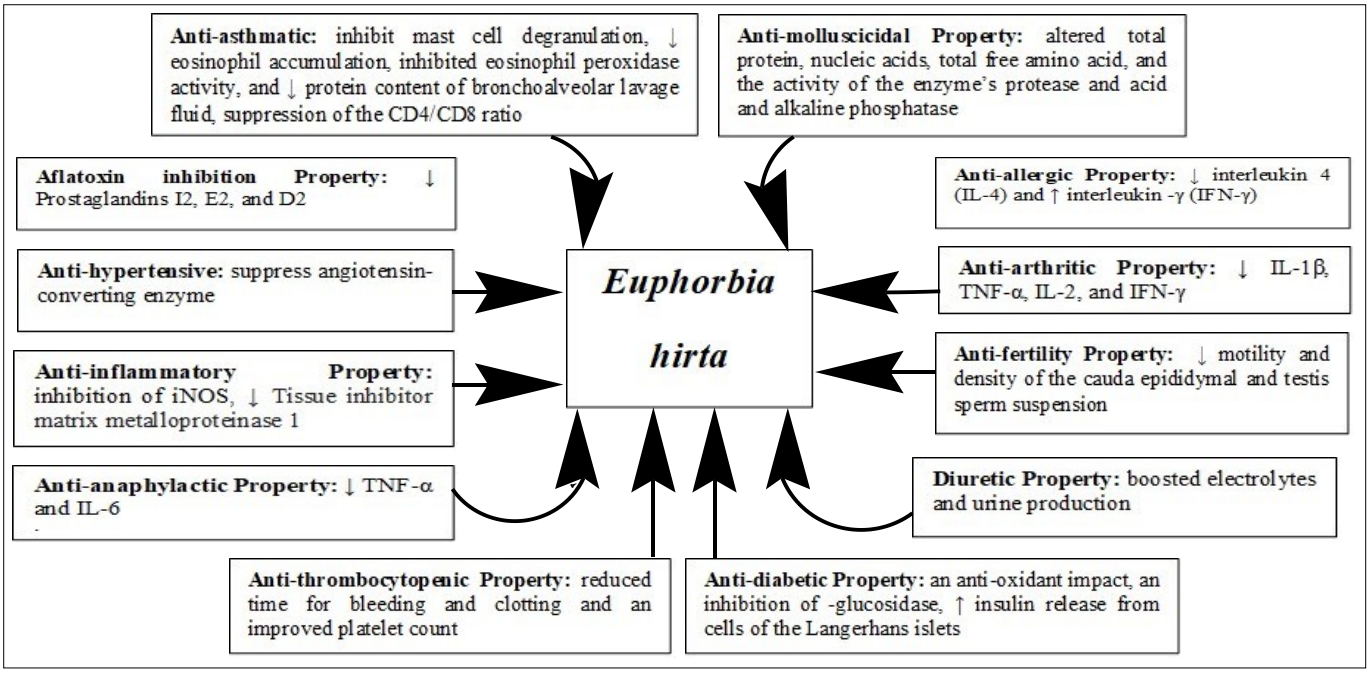


Fig. 2. Pharmacological profile of *E. hirta.*

and 0.01 respectively), *E. hirta* whole plant (HE) demonstrated hepatoprotective effects at doses of 125 mg/kg and 250 mg/kg. Compared to control CCL4 or rats that had been wounded by paracetamol. The hydroalcoholic extract, which was efficacious at doses of 75 mg/kg and 150 mg/kg for hepatoprotective activity in CCL4 and paracetamol injured rats, was the component of the plants that demonstrated the highest level of antihepatotoxic activity in subsequent investigations. The HE demonstrated a 70 and 80% hepatoprotection compared to silymarin's 80 and 90% in trials comparing the HE (125-250 and 75-150 mg/kg) to a reference antihepatotoxic drug (CCL4 or paracetamol-injured rats respectively). This research showed that the hydroalcoholic extract of *Euphorbia hirta* and *Boerhaavia diffusa* was successful in preventing toxic hepatitis in the liver (28).

Anthelmintic and Molluscicidal Property

The plant's aqueous extract showed potential as an anthelmintic agent and decreased the number of helminth eggs found in the faeces of Nigerian dogs.

The petroleum ether extracts of *E. hirta* were examined for their capacity to kill larvae using the late 4th instar larvae of *C. quinquefasciatus* and *A. aegypti* L. Larval mortality was found after exposure for 24 hrs. The LC50 value for *E. hirta* petroleum ether extract was 424.94 against *C. quinquefasciatus* and 272.36 against *A. aegypti* (29, 30).

The latex was thought to be effective against plant-derived snails as a molluscicide (31).

Anti-anaphylactic and Anti-allergic Property

Against compound 48/80-induced systemic anaphylaxis, *E. hirta* ethanolic extract taken orally (100 to 1000 mg/kg) was effective. According to the research, ethanolic extract prevented active paw anaphylaxis in mice and rat passive cutaneous anaphylaxis (PCA). The findings also showed that anti-DNP-HSA stimulation of rat peritoneal mast cells had a suppressive effect on the release of TNF-α and IL-6. Thus, anti-anaphylactic activity of *E. hirta* was reported earlier (24).

Anti-allergic reactions were described earlier. The complete aerial portions of *E. hirta* were used to create a 95% ethanolic extract. 95% ethanolic extract significantly decreased both the edoema caused by dextran and the degranulation caused by compound 48/80 in rat peritoneal mast cells. It decreased the protein content of BLF and inhibited eosinophil accumulation and eosinophil peroxidase activity (BALF). In peripheral blood, extract decreased the CD4/CD8 ratio. Additionally, it reduced the release of IL -4 and increased the production of IFN-γ in ovalbumin-sensitive mice splenocytes. These results proved that *E. hirta* exhibit strong anti-early and late-phase allergic reaction activity when compared to recognised drugs such ketotifen, cetirizine and cyclophosphamide (32).

Anti-arthritic Property

A study was conducted to look at the anti-arthritic effects in an animal model. *E. hirta* may have alleviated adjuvant-induced arthritis, according to the findings. Adjuvant arthritis was brought on by injecting 0.05 ml of newly made *Mycobacterium tuberculosis* suspension (5.0 mg/ml) in liquid paraffin under the plantar surface. Treatment consisted of administering ethanol extract at various concentrations of 25, 50, 100 and 200 mg/kg. According to the findings, *E. hirta* dramatically decreased interleukin -1β, IL-2, Tumor necrosis factor-α and IFN-γ in splenocytes from arthritis-prone mice and downregulated nitric oxide generation in peritoneal macrophages induced by lipopolysaccharide. These findings imply that *E. hirta* has a better response to adjuvant-induced arthritis (33).

Anti-bacterial / Anti-fungal activity

Salmonella typhi, Gram-positive *Staphylococcus aureus* and Gram-negative *E. coli* were isolated by researchers from deteriorated wounds, stool samples and high vaginal swabs. Total dehydrogenase activity was assessed using TTC, the ethanolic inhibitory effects of *E. hirta* and *Euphorbia hyssopifolia* and the common antibiotics ciprofloxacin and gentamycin. Although it is ineffective against *Staphylococcus aureus*, *E. hirta* is efficient against Gram-negative *Escherichia coli* and *Salmonella typhi*. As a result, *E. hirta* may be effective in treating urinary tract infections and typhoid fever (34).

In another study, it was found that fresh and dry leaf extracts (ethanol and water) had antibacterial activity against a numerous of pathogens, including *E. coli*, *Haemophilus influenzae, Klebsiella pneumonia, Proteus vulgaris, Pseudomonas aeruginosa, Slamonella typhi*, *S. aureus, E. hirta* decoction demonstrated little to no zone of prevention against *Haemophilus influenzae*, according to an antibacterial sensitivity test. Therefore, compared to fresh extracts, dry extracts provided the largest zone of inhibition on all pathogens (35).

Using the paper disc diffusion technique, an ethanolic extraction has shown antifungal activity against the plant diseases *Botryodiplodia theobromae, Colletotrichum capsici, Alternaria alternata, Penicillium citrinum, Phomopsis caricae-papayae* and *A. niger* (36).

Anti-cancer Property

Using a brine shrimp lethality assay, the cytotoxicity of *E. hirta* was examined. The results showed that the LC50s of acetone and ethyl acetate extraction of plant components were 71 and 92 g/ml respectively (92). Afzelin, myricitin and quercetin were isolated from the methanolic extraction of leaf and stem of the plant and a different investigation found that they had a negligible cytotoxic impact on human epidermoid carcinoma KB 3-1 cells (70). Leaves of the plant shown toxicity when *in vitro* testing was done on the T-cell from the cells of the blood (37).

The cell line was used to conduct cytotoxicity tests on the extracts and the extract's non-cytotoxic concentration was examined for antibacterial activity in case of cytotopathic concentration of the pathogen. The plant is excellent in treating malignancies, especially squamous cell carcinomas and malignant melanomas (38).

Anti-diabetic Property

The anti-diabetic characteristics of the plant's ethanolic and ethyl acetate decoction were investigated *in vitro* us-

ing the alpha-glucosidase inhibitor method and an *in vivo* oral glucose tolerance test employing various loading protocols was carried out to arrive at a conclusion (39). The method involves several activities, including an antioxidant effect, inhibition of alpha-glucosidase and an increase in the activity of insulin release from Langerhans islet cells (40). Ethanol extracts of *E. hirta* leaf, blossom and stem significantly reduced blood glucose levels in streptozotocin-induced diabetic mice (41). Potential antidiabetic properties of the flower's ethanol and petroleum ether decoctions were also seen in the alloxan- persuaded diabetic animal (42). On rats that had developed diabetes after being exposed to alloxan, the ethanolic extract significantly reduced blood glucose levels (43).

Anti-diarrheal and Anti-spasmogenic Property

The plant's aqueous decoction considerably reduced the impact of castor oil-induced diarrhoea in mice and gastrointestinal motility in normal rats (44). *E. hirta's* water extract has anti-microbial, anti-diarrheal, anti-tetanic and anti-amoebic qualities. Research examined the whole aqueous extract of leaves' ability to contract in rats. The study's findings showed that water extracts had antidiarrheal and spasmogenic effects *in vivo* (45).

Anti-fertility Property

At a concentration of 50 mg/kg b.wt., the plant extract drastically decreased the motility and concentration of the cauda epididymal and testis sperm suspension, resulting in 100% sterility (46).

ACE inhibition Effect /Anti-hypertensive

The study found that the angiotensin-converting enzyme was suppressed by the extract of the plant components (ACE) (47, 48). Using an ELISA, the methanolic decoction of *E. hirta*'s leaves and stem reduced the activity of the ACE by 50% and 90% at 160 and 500 g respectively. Rats' water intake was dramatically reduced when the extract was given intraperitoneally at a concentration of 10 mg/100 mg b.wt. (49).

Anti-inflammatory and Analgesic Property

In a carrageenan-induced edema test in rats, a research investigation found that the aqueous decoction of *E. hirta* displayed strong and concentration-dependent anti-inflammatory properties starting at a level of 100 mg/kg b.wt. (4). About 58.1% and 56.7 % of the increased paw thickness was inhibited by aqueous and ethanolic extract respectively. However, when compared to solvent control, ethanolic extract generated a 57.1% suppression of inflammatory rise in the paw thickness and aqueous extract caused a 54.3% inhibition at a dose of 200 mg/kg b.wt. (50).

Fruit extracts in petroleum ether, chloroform, water, ethanol and methanol were examined for their ability to reduce inflammation. In comparison to other decoctions, the water and ethanol decoctions demonstrated the highest proportion of protection against inflammation (14, 51).

In animal models, an ethanolic decoction (95%) of *E. hirta* aerial parts displayed anti-inflammatory properties. The TPA persuades edema model in mice was utilised to evaluate the effects of an n-hexane decoction of *E. hirta* aerial parts. The main triterpenes found in aerial parts of *E. hirta*, are β-amyrin, 24-methylencycloartenol and b-sitosterolare found to be more effective in the prophylaxis of inflammation. In the TPA persuade edema model, the extract and the triterpenes both exhibited notable concentration-dependent anti-inflammatory effects. The triterpenes were evaluated as anti-inflammatory compounds in dual and triplet forms. The findings demonstrated that the anti-inflammatory effects of the combinations were greater than those of the individual triterpenes alone (52).

In a well-established inflammation model using lipopolysaccharide activated macrophage cells (RAW 264.7), the bioactive ingredients from ethanolic decoction of *E. hirta* were investigated. A colorimetric test, western blotting and RT-PCR were used to evaluate the generation of NO and the expression of the iNOS protein and iNOS mRNA after activation (RT-PCR). It was also kept an eye on how much PGE2, TNF-α, and IL-6 was present. According to the findings, the ethanol extract's active ingredient, beta-amyrin, provided a notable anti-inflammatory impact and demonstrated a concentration-dependent suppression of lipopolysaccharide-induced NO with prohibition of iNOS protein. However, the ethanolic extract had no impact on the iNOS gene's expression.

Since the beta-amyrin component inhibit the majority of iNOS protein activities and NO induction, they may represent novel selective NO inhibitors with significant therapeutic promise for the management of arthritic inflammation (53).

The histopathology of rats given intermediate and low dosages of *E. hirta* exhibited improvement. TIMP-1 levels were shown dose dependent effect, whilst MMP-13 levels were shown to decrease with reducing concentration of *E. hirta* (54).

An aqueous lyophilized extract of *E. hirta* was examined for its antipyretic, analgesic and anti-inflammatory effects on mice and rats. It produced central analgesic effects at doses of 20 and 25 mg/kg and showed a concentration-dependent response to stimuli in the writhing test and hot plate test. Themorphine antagonist chemical naloxone, used as a pretreatment, prevented the analgesic effect. At dosages of 100 and 400 mg/kg, an antipyretic action was seen in yeast-persuade hyperthermia (55).

Anti-malarial Property

Afzelin, quercitin and myricitin, three isolated flavonols glycosides, were shown to suppress *Plasmodium falciparum* growth in a scientific investigation (56). The antimalarial phenomenon of the *E. hirta* decoction was tested in mice infected with *P. berghei* at dosages of 200, 400 and 800 mg/kg b.wt. When compared to chloroquine, which exhibited repressive and preventative anti-plasmodial activities of 95 and 81% respectively, the decoction demonstrated significant (P 0.05) repressive activity of 51 to 59% and preventive activity of 25 to 50% (57).

Anti-microbial and Anti-fungal Property

Anti-microbial study of *E. hirta* leaf decoction suppressed the growth of *S. aureus, P. aeruginosa, T. mentagrophytes* and *Candida albicans* with activity indices of 0.2, 0.3, 0.4 and 0.2 respectively (37).

Methanol, acetone, ethyl acetate and hot aqueous extracts of *E. hirta* (0.02-1.66 mg/ml) were tested for their ability to combat multidrug-resistant (MDR) pathogens. All leaf extracts were effective at killing the studied pathogens, although a methanolic extract of the leaves had the strongest antibacterial phenomenon on *S. aureus, P. aeruginosa* and *E. coli* (inhibitory diameters of 22, 23 and 25 mm respectively) (58).

By using the agar well diffusion method, the ethanol extract of *E. hirta* leaves was examined for its antimicrobial phenomenon against the following bacterial strains: *S. aureus*, *B. ceresus, S. typhi*, *Klebsiella pneumoniae*, *P. aeuroginosa*, *A. niger*. Significant antibacterial activities were demonstrated by the ethanolic extract of *E. hirta* leaves (59). The antibacterial activity of *E. hirta* against *E. coli* and *Klebsiella pneumoniae* was assessed using the agar well diffusion method. Several Gram-negative bacteria, including *Shigella dysentriae, S. typhi* and *Proteus mirabilis* regularly cause gastrointestinal infections in people.

The range for both the minimal bactericidal concentration and the minimal inhibitory concentration was 25 to 100 mg/ml. All the bacteria's development was slowed down in different ways (60).

The antibacterial and antifungal properties of leaf extracts from *E. hirta* in aqueous and organic solvents were investigated against different bacterial species (*Pseudomonas putida, Klebsiella pneumoniae, Pseudomonas aeruginosa, Aeromonas liquefy*, *A. niger, A. flavus, A. fumigatus, A. erythrocephalus* and *Fusarium spp.*). Except for water and butanol extracts, which exhibited no antibacterial action against *Klebsiella pneumonia* and *Aeromonas liquefaciens*, all extracts had antibacterial activity against the studied microorganisms. However, against *Pseudomonas putida, Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Aeromonas liquefaciens* respectively, ethanol extracts demonstrated the maximum activity (14, 12, 12, 14 mm).

Contrarily, ethanolic, butanolic and benzene extraction of *E. hirta* demonstrated the most activity against *A. fumigatus* (13 mm), *A. flavus* (12 mm) and *A. erythrocephalus* (16 mm) respectively (61). *E. hirta* leaves, stems, flowers and roots were used to test the antimicrobial effects of the extracts against nine bacteria, four of them are Gram positive (*Micrococcus sp., S. aureus, B. thuringensis* and *B. subtilis*), other four are Gram negative (*E. coli, Klebsiella pneumonia, P. mirabilis* and *S. typhi*) and one yeast (*C. albicans*). With greater zones of inhibition (18–28 mm), leaf extract reduced the development of all examined microorganisms. When compared to stem extract, root extract had bigger inhibition zones and showed greater activity against Gram positive bacteria. *P. mirabilis* (50 mg/ml), *S. aureus* (12.5 mg/ml) and *E. coli* and *C. albicans* (3.12 mg/ml) had the lowest MIC values. The MIC values for all other microorganisms were 100 mg/ml. According to investigations utilising scanning electron microscopy, the cells exposed to leaf extract had a rough surface with numerous mixing and invaginations, which developed with increasing length of treatment. Cells treated to leaf extract for 36 hrs exhibited severe damage and a profusion of surface fissures that may be linked to eventual cell death and function loss (62). The methanol extract of *E. hirta* demonstrated a strong antibacterial activity (MIC 0.25 mg/ml against *Klebsiella pneumonia* and *E. coli* (63). Researchers tested the antibacterial effects of *E. hirta's* ethanol and petroleum ether extracts on *S. aureus, S. typhi, Pseudomonas aureginosa, Vibrio cholera* and *E. coli*. We examined crude drug concentrations at 25, 50, 75 and 100 g/ml. The outcome demonstrated that leaf, stem, root and bud extracts in ethanol and petroleum ether were effective against the investigated bacteria. On the other hand, ethanol extracts of *E. hirta* may be harmful to microorganisms (64).

Anti-oxidant Property

The DPPH assay and the cyanoferrate method were employed to test the antioxidant and reducing power of the leaves, blossoms, stems and roots of *E. hirta*. The DPPH scavenging activity was found to be highest in leaves than blossoms, roots and stem. The relative IC50 values for the plant's leaves, roots, flowers, stems and butylated hydroxy toluene (BHT) were 0.803 mg/ml, 0.989 mg/ml, 0.972 mg/ml, 1.358 mg/ml and 0.794 mg/ml. The decreasing power of the leaf decoction was discovered to be concentration-dependent and correspondence to that of ascorbic acid. The methanol decoction of *E. hirta* leaves was subjected to phytochemical analysis, which identified phenolic compounds, alkaloids, terpenoids, tannins, steroids, flavonoids and reducing sugars. *E. hirta* may have potent antioxidant properties, according to the reports (65). At 100 g/ml it was found that the methanolic extract showed a DPPH scavenging activity and a hydroxyl radical scavenging activity of 89.75 0.032% and 83.5 0.046% respectively. Significant *in-vivo* antioxidant activity was demonstrated by the ethyl acetate fraction for superoxide dismutase, glutathione, lipid peroxidation and catalase activity (66).

Reports are on the anti-diabetic and antioxidant effects in mice (1). For 3 weeks, alloxan-persuade diabetic mice were given oral tests of *E. hirta* flower extracts in ethanol (250 mg/kg) and petroleum ether (500 mg/kg). Significant reductions were observed in the levels of serum triglycerides, creatinine, alkaline phosphatase and urea. Total proteins and HDL levels rose following therapy. All extracts demonstrated antioxidant activity in the antioxidant experiments. The flower extract from *E. hirta* has anti-diabetic and antioxidant properties (67).

Anti-thrombocytopenic Property

As a potential helpful herb in therapy, Euphorbia's ability to increase platelets was investigated due to thrombocytopenia. In a study, anagrelide was given orally in concentration of 0.083 mg/kg b.wt. to rats to reduce their platelet count. For nine days, a lyophilized aqueous plant sample solution was given. On the tenth day, blood samples were collected for platelet counts both before and after the

treatment. According to the findings, *E. hirta* extracts significantly increased platelet activity (P 0.05) (68).

In another study on Sprague-Dawley rats, the antithrombocytopenic properties of the plant's lyophilized extracts were studied. Within seven days, rat thrombocytopenia was brought on by ethanol extracts. Following the therapy, there was a noticeably reduced time for bleeding and clotting and an improved platelet count (69).

Anti-tumor Property

In an animal model, the anti-tumor effects of *E. hirta* leaves were investigated against the EL-4 cell line. The mean survival period of tumor-bearing animals treated with EF was increased, and the bulk of solid tumours were significantly decreased (70). Human laryngeal epithelioma Hep-2 cells treated with methanolic decoctions of plant leaves exhibited anti-proliferative action (71).

A new cylclopentanone derivative isolated from *E. hirta*, designated (1'R,5'R)-5-(5'-carboxylmethyl-2'-oxocyclopentyl)-3Z-pentenyl acetate (72). The structure was determined using 1D and 2D NMR spectroscopic investigation. The cytotoxicity of an ethanol extract was assessed against the lung cancer cell line A549 and the human leukaemia cell line K562. According to the statistics, the ethanol extract was inert against K562 cells and only moderately active against A549 cells (15.02 11.60%) (72).

Anti-venom Property

The methanolic extract of *E. hirta* was tested against the venom of *Naja naja* snake for its ability to inhibit proteases. There was a significant amount of polyphenol content, including quinic acid, gallic acid and ellagic acid. These bioactive substances may stop venom proteases in their tracks. With 50 mg of venom, a zone of clearance of 1172 mm was achieved in the casein-agarose plate experiment, indicating 100% activity of the venom protease. In a ratio of 1:10 (venom:plant w/w), the extract showed 50% suppression of the venom proteolytic activity and at a ratio of 1:10 it showed total (100%) inhibition. At 0.5 and 1.0 mg of plant extract respectively, the enzymatic activity of the venom was 50% and 100% inhibited, whereas 94% inhibition was seen when the venom was incubated with AV (1:60 w/w) (73).

Anti-viral Property

On MT4 human T-cell line the aqueous and methanol extract of the plants were investigated against various virus species including HIV-1 and 2 as well as SIVmac251 for the antiretroviral activity. The inclusion of the active component tannin in 50% methanolic decoctions, which demonstrated higher anti-retroviral efficacy than water extract, was primarily responsible for this (74).

Anxiolytic and Sedative Effect

E. hirta hydroalcoholic (Eh) extract's anxiolytic effects were investigated earlier. Stress was brought on in rats using forced swimming stress (FSS) and chronic immobilisation (CIS). After using Eh (200 mg/kg orally) for 7 days, the activity in CIS and FSS significantly decreased and anti-anxiety effects were clearly visible. Flumazenil (500 µg/kg intraperitoneal) and bicuculline (1000 µg/kg intraperitoneal) were administered to rats in combination and this significantly reduced the anxiolytic effect of Eh. This shows that the benzodiazepine receptor, Gamma-aminobutyric acid A receptor and Cl^-channel complex are involved in the medication of anxiolytic action. As a result, Eh functions as a possible anxiolytic medication, which may be helpful in treating anxiety disorders brought on by stress. *E. hirta* had behavioural impacts on mice, according to Marie-Claire Lanhers et al. in 1990. When supplied intravenously and orally, lyophilised aqueous extract did not exhibit any mortality. By using an activity test and a staircase test at the highest (100 mg/kg) and lowest (12.5 and 25 mg/kg), behavioural parameters were decreased and enhanced. These results corroborate *E. hirta's* historical use as a sedative and anxiolytic (14).

Corrosive Property

Research was conducted to see how well the plants prevented rusting. For the investigation, a gravimetric method was employed. In both acidic and alkaline settings of 0.5 M HCl and 0.25 M NaOH, respectively, the extract from the leaf material under study was found to be an efficient green inhibitor of aluminum alloys corrosion. The adsorption of the organic extract on the surface of the aluminum alloy and the blockage of active sites prevented corrosion in an acidic environment. A thorough analysis of the data produced some intriguing findings. The extract prevented the corrosion of aluminum alloys in acidic conditions by impeding both cathodic and anodic electrode processes; the extract's effectiveness in preventing corrosion increased with the number of bonds it contained. It was discovered that temperature, exposure period and inhibitor concentration primarily regulated the inhibitor's ability to inhibit. The inhibitor was discovered to follow the Temkin adsorption isotherm in the alkaline solution as well as the physisorption-based Langmuir adsorption isotherm in both acidic and alkaline media (75).

Diuretic Property

An animal model's diuresis was considerably affected by the ethanol and water extracts of *E. hirta* leaf, according to research. It boosted electrolytes and urine production. The results of the studies demonstrated that the main active ingredients in the leaf's aqueous extract have potent diuretic efficacy similar to that of acetazolamide (17). It was used the common diuretics acetazolamide and furosemide to study the diuresis efficacy of leaf decoction of *E. hirta* in rats. With aqueous and ethanolic decoction (50 and 100 mg/kg), a time-dependent increase in urine production was seen. According to the findings, water extracts enhanced urine output and acetozolamide-like increases in sodium, potassium, and bicarbonate excretion in the urine. The excretion of bicarbonate was enhanced, the loss of potassium was decreased and the elimination of sodium was only slightly affected by ethanol extract. Furosemide, the conventional medication, enhanced the renal excretion of sodium and chloride but had little impact on the loss of potassium and bicarbonate. These findings confirm the Swahili and sukumus' historic usage of *E. hirta* as a diuretic (45).

Effect on Asthma

In animal models, 95% ethanolic decoction of entire aerial portions of *E. hirta* exhibited antihistaminic and immunosuppressant effects. It prevented the mast cell degranulation in rat. In case of mild asthma, it avoided the accumulation of eosinophil, inhibits the activity of enzyme eosinophil peroxidase, and also decreases the content of protein which is present in BAL fluid. In mouse splenocytes that had been exposed to ovalbumin, ethanolic decoction also reduced the release of IL-4 and increased the production of interferon (32). With *E. hirta* at 50 mg/kg, mast cell disruption was 29.802% while intact mast cell percentage was 71.202%. However, at a concentration of 100 mg/kg b.wt., which was comparable to the standard prednisolone, 24.70% of the mast cells were destroyed and 81.10% were intact (76).

The plant's antispasmodic characteristics were tested against cholinergic and histaminic drug-induced contractions on smooth muscle (trachea) and it exhibited completely reversible direct muscular activity. This enables researchers to identify whether Euphorbia's antispasmodic activity is myotropic or neurotropic. It had negligible to no relaxing effects on normal muscle (77). Using a mouse Balb/c asthma model, performed a relative ultrastructural investigation of platelet and fibrin connections (78). When asthmatic mice were given two doses of hydrocortisone and one dose of plant extract, the ultrastructure of their fibrin connections and platelets was compared to that of control mice. Control mice have firmly spherical platelet aggregates with the development of pseudopodia, minor, thin and major, thick fibres. Large fibrils with tiny, net-like fibres and loosely linked, granular platelet aggregates are present in asthmatic mice. While hydrocortisone, at both doses, made the fibrin more fragile and caused more granular platelet aggregation, *E. hirta* had no effect on the stiffness of the fibrin and inhibited the tiny fibres from creating a compact webby layer over the large fibres (78).

Effect on CNS

An investigation looked at the plant's aqueous extract for potential benzodiazepine-like, neuroleptic, antidepressant and hypnotic effects. The plants decoction had a little antidepressant effect and had a direct effect on the central nervous system (14).

Galactogenic Property

Prior to puberty, the dried plant powder was administered to female guinea pigs, and the results of the study revealed that it promoted milk production and accelerated mammary gland growth (79).

GI Tract Effect

A study was conducted to look at the animal GI motility. Results demonstrated that Castrol oil-induced diarrhoea in mice and a substantially and dose-dependent reduction in gastro-intestinal motility in rats were both caused by water extract of leaves (44).

Genoto-toxic Effect

Using the Allium cepa test, research analysis revealed that methanolic extract had genotoxic properties. The study's findings showed that the methanolic extraction of *E. hirta* (1000 µg/ml) had strong mitotoxic and genotoxic effects (80).

Hepato-protective Property

The anti-hepatotoxic characteristics of the plant's hydroalcoholic decoction were assessed using animal models of liver damage brought on by CCl4 or paracetamol (81). The animals given the extracts had significantly lower blood levels (125 mg/kg and 250 mg/kg) as compared to CCl4 or paracetamol-injured mice (P 0.05 and 0.01 respectively) (82).

Herbicidal Property

A study looked at how *E. hirta* affected the germination and development of groundnut seedlings. Compared to lower doses, higher amounts greatly inhibited germination. Groundnut shoots and root length dramatically decreased in soil that was infested with *E. hirta* (83).

Immunomodulatory Property

By inhibiting NO generation, the plant extract is said to have 45% immunomodulatory capabilities (84). According to research, the plant exhibits *in vitro* and *in vivo* immunomodulatory capabilities that have been demonstrated using carbon clearance technique, mast cell de-granulation assay, and macrophage impact testing (85, 86).

Sperm Motility Effect

In a study, healthy, sexually mature West African Dwarf rams were used. The outcome suggests that the viability and fertility of spermatozoa were adversely impacted.

West African Dwarf (WAD) rams that were sexually mature and in good health were used (87). The rams used in the study were between 24 and 30 months old. Test animals received 400 mg/kg b.wt. orally throughout the course of 14 days. Following a one-day and seven-day treatment period, semen samples were taken. The live-dead ratio declined from 90.75% to 32.5% and sperm motility in the semen image decreased significantly from 80% to 47.5% (p 0.05). This data suggests that the ability of spermatozoa to survive and reproduce was compromised. The numbers for the body's parameters, however, did not show any noticeable alteration. As a result, it was suggested against using *E. hirta* as medicine on animals that were male (87).

Synergistic Property

Erythromycin and methanolic decoctions of *E. hirta* leaves were tested for their combination anti-*Staph aureus in vitro* action. The results showed a synergistic interaction between erythromycin and the leaves of *E. hirta* (88).

Wound healing Property

Rats with excision wounds (500 mm^2 of the anterio-dorsal side skin removed while under anesthesia) were tested for wound-curing properties of ethanolic leaves from *E. hirta*. An ointment containing the extract was created (5% and 10% W/W). Various periods of time were used to observe the wound contraction. Significant (P 0.001) wound contraction was seen with *E. hirta* leaf extracts at both concentrations (89). Rats with burn wounds were used to test the

effectiveness of 2% w/w cream containing a complete *E. hirta* ethanol extract. Animals treated with *E. hirta* showed considerable burn wound curing activity as measured by the % reduction in the initial wound (90).

Toxicity data associated with Euphorbia hirta

For a very long time, *E. hirta* has been utilised in folk medicine. Target organ toxicity has only sometimes been reported in the literature, and there hasn't been much study done on how safe and hazardous the plant is. A 38-week-old mature male was given 400 mg/kg of aqueous extracts orally to show how the extract affected the male genitel organs. The findings demonstrated that varying testicular degeneration dosages brought on by the decoction lowered the average seminiferous tube diameter in the subject animals (3, 91). The amounts of protein, nucleic acids, free amino acids and the characteristics of the enzyme's acid phosphatases, enzymes proteases and alkaline phosphatases were altered in several tissues of the vector snail *Lymnaea acuminata* by sub-lethal dosages of the decoction in time- and dose-dependent patterns (32). Toxicology of the plant decoction was the subject of another inquiry. According to the findings, all plant sections other than the flower exhibited LC50 values of almost l mg/ml (62, 71). It was examined how well dried sections of *E. hirta* latex combined with additional active ingredients including ellagic acids, teraxerol, rutin and betulin performed in binary and tertiary combinations. Fresh water snails *Indoplanorbis exustus* and *Lymnaea acuminata* were chosen as targets for the latex and active chemicals' toxic effects in the pond. Snails and the fish *Channa punctatus* were both fatal to large doses, although LC90 had no such effects on fish (92).

Animals receiving a single dosage of 5000 mg/kg of the plant's methanol extract were not affected by the acute or subchronic oral toxicity of the substance. Over 5000 mg/kg was thought to be the LD50. The administration of the plant extract at doses of 50, 250 and 1000 mg/kg/day did not significantly vary from the control group in the repeated dosage 90-day oral toxicity inquiry study ($P > 0.05$) and did not result in sub-chronic toxic effects. Animal tests were conducted on the plant's ethanol extract. Animals received ethanolic extract at doses of 200, 400 and 600 mg/kg for 14 days. According to the findings, the plant significantly increased (P 0.05) the levels of RBC, WBC, platelets, hemoglobin and PCV while causing a decrease in lymphocytes. When compared to normal controls animals, the serum lipid profile of *E. hirta* extract significantly reduced (P 0.05). The levels of ALT and AST features in the treatment group somewhat increased in comparison to the control group (93, 94).

Conclusion

The current review reveals all scientific research conducted on *E. hirta* and its bioactive compound which gives a brief review of plants pharmacological action and its phytoconstituents. *E. hirta* L. has been traditionally employed to manage a wide range of disorders. Furthermore, various animal research investigations have proved its applications beyond ethnomedicinal ones. Several pharmacological benefits of this plant have been researched, including hepatoprotective, antifertility, analgesic, antidiabetic and anti-inflammatory, antioxidant, hypolipidemic, antiallergic, antihypertensive, antispasmodic and anticancer, immunomodulatory and many more. Therefore, we will be able to decoct phytopharmaceuticals in a purer form which has high therapeutic efficacy and can be employed as a novel target for the management of a number of diseases. Phytopharmacology of various extracts, standardization of extracts, isolation and characterization of active phytopharmaceuticals, elucidation of the action mechanism of isolated compounds and clinical trials of that isolated compounds are all essential phases in the development of high-quality herbal medications.

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Authors contributions

In the present review, SC analyzed the data related to disease and treatment approaches with Bioactive compounds and was the most important contribution in making the manuscript. SD, AM, N and VSC performed the systematic evaluation and elaborated on the conclusion. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: The authors declare that they have no competing interests.

Ethical issues: Not applicable.

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